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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/667,004	CHAN ET AL.	
	Examiner	Art Unit	
	Frank W. Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *25-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/04 and 6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-24 and species (2) (the target molecule is a nucleic acid or polynucleotide or an oligonucleotide (claims 3, 4, 6-8, 15, 16, and 22)) in the reply filed on April 25, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Therefore, claims 1-24 will be examined.

Specification

2. The disclosure is objected to because of the following informalities: (1) "SPM" in abstract in page 41 should be "scanning probe microscopy (SPM)"; and (2) there are Figures 2A and 2B. However, there is no description for Figure 2B in Brief Description of the Drawings of the specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 11, 13, 14, 21, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 11 recites the limitation "the scanning probe microscopy technique" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no scanning probe microscopy technique in claims 1 and 10. Please clarify.

6. Claim 13 recites the limitation "the sequences of oligonucleotides that binds to the nucleic acid" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no oligonucleotides and nucleic acid in claims 1, 9, and 12. Please clarify.

7. Claim 21 recites the limitation "the scanning probe microscopy technique" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no scanning probe microscopy technique in claim 19. Please clarify.

8. Claim 24 is rejected as vague and indefinite. Since step c) of claim 19 requires aligning on a surface the coded probes that bind to the one or more target molecules while claim 24 requires separating the bound coded probes from the target molecules before the coded probes are aligned on a surface, if the bound coded probes are separated from the target molecules before the coded probes are aligned on a surface as recited in claim 24, it is unclear how to align on a surface the coded probes that bind to the one or more target molecules. Therefore, claims 19 and 24 do not correspond each other. Please clarify.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-6, 9, and 15-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Mirkin *et al.,* (US Patent No. 6,361,944 B1, filed on June 25, 1999).

Regarding claims 1-3, 6, 15, and 16, since Mirkin *et al.,* teach to hybridize SEQ ID NO: 33 immobilized on a nanoparticle which is on a substrate to a linking oligonucleotide comprising SEQ ID NO: 34, and then hybridize a complex formed by SEQ ID NO: 33 and the linking oligonucleotide comprising SEQ ID NO: 34 to SEQ ID NO: 35 immobilized on a nanoparticle (see Example 6 in pages 50 and 51, and Figure 13B), Mirkin *et al.,* disclose obtaining one or more coded probes (eg., SEQ ID NO:33 and SEQ ID NO:35), each coded probe comprising a probe molecule attached to at least one nanobarcode (ie., nanoparticle), contacting a target molecule (eg., the linking oligonucleotide comprising SEQ ID NO: 34) with the coded probes, and organizing the coded probes that bind to the one or more target molecules (ie., forming nanoparticle aggregates linked to substrate by analyte DNA) as recited in steps a) to c) of claim 1 wherein each coded probe comprises an oligonucleotide as recited in claim 2, the target molecule is a nucleic acid as recited in claim 3 or 16, the nucleic acid is attached to a surface as recited in claim 6, and identifying the nucleic acid from the coded oligonucleotide probes that bind to the nucleic acid as recited in claim 15. Since Mirkin *et al.,* teach to identify hybridization complex formed by SEQ ID NOs: 33-35 by UV-vis absorbance (see column 50 and Figure 14A), Mirkin *et al.,* disclose identifying the organized coded probes and detecting one or more the target molecules based on the bound coded probes (ie., detecting the hybridization between the target molecule and the coded probes) as steps d) and e) of claim 1.

Regarding claims 4 and 5, Mirkin *et al.,* teach that a library of coded probes comprising

all possible sequences for a particular length of oligonucleotide is contacted with the target molecule as recited in claim 4 wherein the nanobarcode is nanoparticles as recited in claim 5 (see Figures 17A to 17C).

Regarding claim 9, Mirkin *et al.,* teach further comprising aligning the coded probes on a surface by molecular combing as recited in claim 9 (see Figure 21).

Regarding claims 17 and 18, since the target nucleic acid used in the assay taught by Mirkin *et al.,* comprises multiple identical molecules, Mirkin *et al.,* teach further that two or more target molecules are present in a sample and all target molecules in the sample are analyzed at the same time as recited in claim 17 and two or more target molecules are present in a sample and all target molecules of the same kind are analyzed at the same time as recited in claim 18 (see Figures 20 B, 21 and 22).

Therefore, Mirkin *et al.,* teach all limitations recited in claims 1-6, 9, and 15-18.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin *et al.*, (1999) as applied to claims 1-6, 9, and 15-18 above, and further in view of Birkenmeyer *et al.*, (US Patent No. 5,427,930, published on June 27, 1995).

The teachings of Mirkin *et al.*, have been summarized previously, *supra.*

Mirkin *et al.*, do not disclose ligating adjacent coded oligonucleotide probes that are hybridized to the nucleic acid or target molecule and separating ligated coded oligonucleotide probes from the nucleic acid or target molecule and non-ligated coded oligonucleotide probes as recited in claims 7 and 8. However, since Mirkin *et al.*, teach to wash the substrate after each hybridization step (see column 50), Mirkin *et al.*, teach separating the coded oligonucleotide probes from the nucleic acid and non-ligated coded oligonucleotide probes.

Birkenmeyer *et al.*, teach filling the gap between two adjacent probes when they are hybridized to a target nucleic acid and separating ligated probes from the target nucleic acid and non-ligated probes (see abstract and columns 2-4). Since Birkenmeyer *et al.*, teach ligating extended probe A to probe B, and extended probe B' to probe A', using said ligase reagent to form reorganized probe molecules, providing denaturing conditions to separate said reorganized probe molecules from said template and separating reorganized probe molecules from unreorganized labeled probes (see column 3), Birkenmeyer *et al.*, disclose claims 7 and 8.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art

at the time the invention was made to have ligated adjacent coded oligonucleotide probes that are hybridized to the nucleic acid or target molecule and separated ligated coded oligonucleotide probes from the nucleic acid or target molecule and non-ligated coded oligonucleotide probes as recited in claims 7 and 8 in view of the patents of Mirkin *et al.,* and Birkenmeyer *et al.*. One having ordinary skill in the art would have been motivated to do so because Birkenmeyer *et al.,* have successfully filled the gap between two adjacent probes when they are hybridized to a target nucleic acid and separated ligated probes from the target nucleic acid and non-ligated probes (see abstract and columns 2-4), and Birkenmeyer *et al.,* suggest that filling the gap between two adjacent probes by a ligase chain reaction creates geometrically increasing numbers of reorganized probe molecules in the presence of said target sequence (see column 2, lines 51-58). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to ligate adjacent coded probes that are hybridized to the nucleic acid in view of the patents of Mirkin *et al.,* and Birkenmeyer *et al.*.

13. Claims 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin *et al.,* (1999) as applied to claims 1-6, 9, and 15-18 above, and further in view of Nygren *et al.,* (US Patent No. 6,060,237, filed on January 17, 1995).

The teachings of Mirkin *et al.,* have been summarized previously, *supra.*

Regarding claims 13 and 14, since Mirkin *et al.,* teach to use their method in sequencing nucleic acid (see column 18, third paragraph), Mirkin *et al.,* must disclose or suggest further comprising determining the sequences of oligonucleotides that bind to the nucleic acid and further comprising determining the sequence of the nucleic acid from the sequences of

oligonucleotides that bind to the nucleic acid as recited in claims 13 and 14.

Mirkin *et al.,* do not disclose that the coded probes are identified by scanning probe microscopy as recited in claim 10 wherein the scanning probe microscopy is scanning tunneling as recited in claim 11 and wherein the coded probes aligned on the surface are identified by scanning probe microscopy as recited in claim 12. However, Mirkin *et al.,* teach to identify the coded probes by transmission electron microscopy (see column 43, first paragraph) or fluorescence microscopy (see column 59, last paragraph).

Nygren *et al.,* teach to detect hybridization by scanning tunneling microscopy (see column 3, fourth paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have identified the coded probes by scanning probe microscopy wherein the scanning probe microscopy is scanning tunneling microscopy as recited in claims 10-12 in view of the patents of Mirkin *et al.,* and Nygren *et al.*. One having ordinary skill in the art would have been motivated to do so because Nygren *et al.,* have successfully detected hybridization by scanning tunneling microscopy and the simple replacement of one well known detection method (i.e., the method taught by Mirkin *et al.,*) from another well known detection method (i.e., detecting hybridization by scanning tunneling microscopy taught by Nygren *et al.,*) during the process of performing the method recited in claims 10-12 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the detection method taught by Mirkin *et al.,* and the detection method taught by Nygren *et al.,* are two functional equivalent methods which are used for the same purpose (ie., detecting hybridization).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06.

14. Claims 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin *et al.,* (1999) as applied to claims 1-6, 9, and 15-18 above, and further in view of Nygren *et al.,* (US Patent No. 6,060,237, filed on January 17, 1995).

The teachings of Mirkin *et al.,* have been summarized previously, *supra.*

Regarding claim 19, since Mirkin *et al.,* teach to hybridize SEQ ID NO: 33 immobilized on a nanoparticle which is on a substrate to a linking oligonucleotide comprising SEQ ID NO: 34, and then hybridize a complex formed by SEQ ID NO: 33 and the linking oligonucleotide comprising SEQ ID NO: 34 to SEQ ID NO: 35 immobilized on a nanoparticle (see Example 6 in pages 50 and 51, and Figure 13B), Mirkin *et al.,* disclose obtaining one or more coded probes (eg., SEQ ID NO:33 and SEQ ID NO:35), each coded probe comprising a probe molecule attached to at least one nanobarcode (ie., nanoparticle), contacting a target molecule (eg., the linking oligonucleotide comprising SEQ ID NO: 34) with the coded probes, and aligning on a surface the coded probes that bind to the one or more target molecules (ie., forming nanoparticle aggregates linked to substrate by analyte DNA) as recited in steps a) to c) of claim 19. Since Mirkin *et al.,* teach to identify hybridization complex formed by SEQ ID NOs: 33-35 by UV-vis absorbance (see column 50 and Figure 14A), Mirkin *et al.,* disclose identifying the aligned coded probes and detecting one or more the target molecules from the identified coded probes (ie.,

detecting the hybridization between the target molecule and the coded probes) as steps d) and e) of claim 19.

Regarding claims 20 and 22, since claims 3 and 9 are identical to claims 20 and 22 respectively, Mirkin *et al.,* teach claims 20 and 22.

Regarding claim 23, since claims 2, 13, and 14 includes all limitations recited in claim 23, Mirkin *et al.,* teach further comprising determining at least part of the sequence of the nucleic acid from the bound coded probes.

Mirkin *et al.,* do not disclose that the aligned coded probes are identified by scanning probe microscopy as recited in step d) of claim 19 wherein the scanning probe microscopy is scanning tunneling as recited in claim 21. However, Mirkin *et al.,* teach to identify the coded probes by transmission electron microscopy (see column 43, first paragraph) or fluorescence microscopy (see column 59, last paragraph).

Nygren *et al.,* teach to detect hybridization by scanning tunneling microscopy (see column 3, fourth paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have identified the aligned coded probes by scanning probe microscopy wherein the scanning probe microscopy is scanning tunneling microscopy as recited in claims 19 and 21 in view of the patents of Mirkin *et al.,* and Nygren *et al.*. One having ordinary skill in the art would have been motivated to do so because Nygren *et al.,* have successfully detected hybridization by scanning tunneling microscopy and the simple replacement of one well known detection method (i.e., the method taught by Mirkin *et al.,*) from another well known detection method (i.e., detecting hybridization by scanning tunneling

microscopy taught by Nygren *et al.,*) during the process of performing the method recited in claims 19 and 21 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the detection method taught by Mirkin *et al.,* and the detection method taught by Nygren *et al.,* are two functional equivalent methods which are used for the same purpose (ie., detecting hybridization).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 5, 9-15, 17, 18, and 28-31 of copending Application No. 10/251,152. Although the conflicting claims are not identical, they are not patentably distinct from each other because an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but examined claims in this instant application are not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although claims 1-23 in this instant application are not identical to claims 1, 4, 5, 9-15, 17, 18, and 28-31 of copending Application No. 10/251,152, claims 1, 4, 5, 9-15, 17, 18, and 28-31 of copending Application No. 10/251,152 are directed to the same subject matter and fall entirely within the scope of claims 1-23 in this instant application. In other words, claims 1-23 in this instant application are anticipated by claims 1, 4, 5, 9-15, 17, 18, and 28-31 of copending Application No. 10/251,152.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

17. No claim is allowed.

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

May 12, 2006

FRANK LU
PRIMARY EXAMINER